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ORIGINAL ARTICLE

Effects of Anti-Tuberculosis Drugs on Lipid Profile in Pulmonary Tuberculosis Patients

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ABSTRACT

Objective: To determine the anti-tuberculosis drugs effect on the lipid profile parameters in pulmonary tuberculosis (TB) patients.

Methods: A prospective cross-sectional study was conducted at Tehsil Headquarter Hospital, Taunsa Sharif and District Headquarter Teaching Hospital, Dera Ghazi Khan from December 2020 to May 2021. The blood samples from 84 positive pulmonary TB patients were collected in three different intervals of the study, before the start of the treatment, and after the use of first four baseline drugs isoniazid (INH), rifampicin (RIF), pyrazinamide (PZA), and ethambutol (EMB) respectively to check out the variation in lipid profile parameters such as total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL), triglyceride (TG) and very low density lipoprotein (VLDL).

Results: Of 84 pulmonary TB patients, the mean age was 38.1 ± 19.8 years. There were 44 (52.4%) males and 40 (47.6%) females. The mean difference of cholesterol level significantly increases from baseline to 6th and 10th week, (p-value <0.001). Similarly, HDL (p-value <0.001) and LDL (p-value <0.001) also increases significantly from baseline to 6th week and 10th week. However, no significant difference of TG (p-value 0.908) and VLDL (p-value 0.367) was observed from baseline to 6th and 10th week.

Conclusion: Patients with pulmonary TB showed low lipid profile in our cohort. This shows that pulmonary TB may be a causative agent of low lipid profile. After anti-TB therapy, cholesterol, HDL, and LDL levels seem to be increased.

Keywords: High-density Lipoprotein, Low-density Lipoprotein, Triglycerides, Total Cholesterol, Tuberculosis, Very low-density Lipoprotein.

INTRODUCTION

Mycobacterium tuberculosis (MTB) has the largest genome of all the obligate human pathogens or in intracellular bacteria.[1] One of the most impressive characteristics of MTB is its ability to trigger a latent infection. Far from the 19th century, when TB was the leading cause of death in Europe's developed nations, the twenty-first century is confronted with a massive reservoir of latent tuberculosis infection (LTBI).[2] A year, more than 1.5 million peoples die from tuberculosis (TB) around the world. In India, about 40% of the population is afflicted with TB bacteria. Per year, it is the second leading cause of death, killing 2 million peoples. Pakistan is a country where TB is both widespread and epidemic.[3] TB is a big public health problem in Pakistan, with the country accounting for one-fifth of all TB incidence cases worldwide.[4]

According to World Health Organization (WHO) report, a total of 186,772 cases were diagnosed with multi drug resistance-TB and rifampicin (RIF) resistant TB, and 156,071 patients began treatment are estimated to appear globally in 2018.[5] Isoniazid (INH) in combination with three other drugs-RIF, pyrazinamide (PZA), and ethambutol (EMB) is the most effective medication for active pulmonary TB. INH is the commonly recommended first-line therapy for TB.[6] Due to hepatotoxicity, one of the main effects of anti-TB drug is on the lipid profile of patients.[7] However, growing evidence suggests that low blood cholesterol is associated with many human diseases including pulmonary TB. Nevertheless, the developing TB diseases are significantly higher when immune systems are poor, particularly patients with human immunodeficiency virus (HIV) infection.[8] The main objective of study is to evaluate the mean difference of variation in lipid profile during TB treatment and also to measure out that which parameter of lipid profile is

mostly affected by anti-TB drugs.

METHODS

A prospective cross-sectional study was conducted at Tehsil Headquarter Hospital, Taunsa Sharif and District Headquarter Teaching Hospital, Dera Ghazi Khan from December 2020 to May 2021. The samples were voluntarily collected from the TB patients for the first time in Pakistan with three different intervals of treatment and the range of their age was 30-70 years. The study was permitted on 15-07-2021 (Ref No: IRB-UOL-FAHS/812-VIII/2021) by the Institutional Ethics Committee and was in accordance with the declaration of World Medical Association (WMA) made at Helsinki (2013). Clinical history of all the patients were taken and then screened the patients for the confirmation of pulmonary TB. The patients with MTB positive results under gene Xpert,[10] were selected for serum lipid profile testing. We collected 3ml of blood samples from MTB positive patients before the start of anti-TB drug treatment. Afterwards, we collected a 3ml of blood sample again on 6th week when patients used the first four baseline drugs INH, RIF, PZA, and EMB. The third sampling was completed whenever patients left the dose of PZA and EMB but still use INH and RIF, in 10th week of the treatment. Sampling of the patients were managed on the change of the anti-TB drugs. All procedures were done under the WHO standard operating procedures (SOPs).

TB infected patients who were confirmed through gene Xpert and acid-fast bacilli test, particularly selected for sampling while the patients with treatment defaults in the first 30 days were excluded. After that we collected the 3ml of blood samples from each diagnosed patient and separated the serum of samples on high gravitational force of centrifuge. Then these serum samples of TB patients were examined on the chemistry analyzer Micro-Lab 300 and Selectra Junior on the principle of Beer Lambert's law. All parameters of lipid profile such as total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL), triglyceride (TG) and very low density lipoprotein (VLDL) were measured enzymatically by DiaSys FS kit on chemistry analyzer. The comparison of diagnostic values of pulmonary TB patients was performed with normal values of these parameters.

Data entry and analysis were done using Statistical Package for Social Sciences (SPSS) version 20.0. Mean ± SD were computed for quantitative variables like, age while frequency and percentages were computed for categorical variables of like, gender. Inferential statistics were explored using paired t-test and repeated measure ANOVA to compare mean difference of lipid profile in pulmonary tuberculosis patients at different time intervals. The p-value of ≤ 0.05 was considered statistically significant.

RESULTS

Of 84 pulmonary TB patients, the mean age was 38.1 ± 19.8 years. There were 44 (52.4%) males and 40 (47.6%) females. The mean difference of cholesterol level significantly increases from baseline to 6th and 10th weeks, (p-value <0.001). Similarly, HDL (p-value <0.001) and LDL (p-value <0.001) also increases significantly from baseline to 6th week and 10th week. However, no significant difference of TG (p-value 0.908) and VLDL (p-value 0.367) was observed from baseline to 6th and 10th week. (Table 1)

Patients of age ≤ 34 years showed the mean difference of cholesterol level (p-value <0.001), HDL (p-value <0.001) and LDL (p-value <0.001) significantly increases from baseline to 6th and 10th weeks. Similarly, in age > 34

Table 1: Mean difference of lipid profile in pulmonary tuberculosis patients before anti-tuberculosis treatment, after 6th and 10th weeks of the treatment (n=84)

	Before Treatment	6th week	10th week	p-value [a]	p-value [b]	p-value [c]	p-value [d]
TC mg/dL	128.07± 33.47	143.13 ± 27.98	145.95 ± 26.77	< 0.001*	< 0.001*	0.141	< 0.001*
TG mg/dL	130.07 ± 52.55	130.05± 28.56	128.84 ± 20.44	0.966	0.846	0.647	0.908
HDL mg/dL	29.31 ± 11.49	35.13 ± 7.30	39.73 ± 6.75	< 0.001*	< 0.001*	< 0.001*	< 0.001*
LDL mg/dL	74.54 ± 22.71	85.41± 23.99	90.40 ± 29.85	< 0.001*	< 0.001*	0.022*	< 0.001*
VLDL mg/dL	24.00 ± 10.61	23.40 ± 6.37	22.67 ± 5.64	0.760	0.302	0.061	0.367

HDL: High density lipoprotein, LDL: Low density lipoprotein, TC: Total cholesterol, TG: Triglyceride, VLDL: Very low density lipoprotein, a= baseline and 6th week, b= before and 10th week, c= 6th and 10th week, d= before, 6th and 10th week (RM-ANOVA) Paired t-test was applied between two groups and Repeated Measure ANOVA was applied among before, 6th and 10th week treatment, *p-value ≤ 0.05

years, cholesterol level (p-value 0.004), HDL (p-value <0.001) and LDL (p-value 0.003) significantly increases from baseline to 6th and 10th weeks. Moreover, a significant mean difference of gender (both male and female) was found with cholesterol level (p-value <0.001) and HDL (p-value <0.001). (Table 2)

DISCUSSION

TB is an epidemic for global public health; this is leading reasons of death from infectious diseases. According to WHO, MTB infects the one third of the world's population. TB is highly infectious in the active state and the respiratory system is its main route of transmission. This disease could be caused through the reduction of about 10 bacteria in the deep lungs.[11]

Our studies appraised that lipids are the most important factor of body nutrition because cholesterol-lowering lipids in the body increases sensitivity for different pathogenic infections, especially with tuberculosis. Cholesterol is a major component of the cell membrane lipid content.[12] This is necessary to maintain the fluidity of the screen.[13] Cholesterol in macrophages is also required for phagocytic activities such as cell magnetism, endocytosis and exocytosis. In deficiency of cholesterol, its phagocytic action is impaired.[14] This study was performed to note any differences in the concentration of the lipid profile (TC, TG, LDL-C, and HDL-C) in TB patients in determining lipid profile levels in response to TB treatment. We performed 84 lipid profile tests of TB patients and samples were collected at baseline and after 6 and 10 weeks of treatment.

In this observational study we see a particular difference in TB patients before and after the treatment. At the end of treatment of tenth week, the levels of TC were increased. Cholesterol, HDL, LDL particularly increased but TG and VLDL value was shortly decreased and becomes normal after 10 weeks of treatment. Similar results were obtained by Sushilendu et al. in 2019,[15] according to their study, TC, HDL and LDL levels were significantly lower in TB patients as compared to normal subjects before and after the treatment. At the end of treatment, the levels of TC remained significantly lower in TB treated patients when compared with the healthy peoples. When compared with the levels before treatment, TC and HDL levels increased significantly after treatment. Studies have shown that MTB has a predominant use of fatty acids over carbohydrates. So, during acute infections, the use of cholesterol by MTB bacilli can lower the host pool. The reason for lowering cholesterol levels in debilitated patients is that it can also cause low production rates and high catabolism during debilitating infections.[16]

We divided our sample size into two groups of ages ≤ 34 years and > 34 years respectively and each group show a significant decrease in cholesterol, HDL and LDL level before the treatment of TB as Vrieling et al. in 2018[17] and Jo et al. in 2021[18] has also reported that low lipid profile specifically low cholesterol level would be an alarming sign for the development of TB. A study in 2005 was conducted by Perez-Guzman and his colleagues showed that an adequate level of cholesterol is necessary for the proper functioning of the immune system against infection because a cholesterol-rich diet accelerates bacteriologic sterilization in patients with TB.[19] This is similar to our result in that HDL levels decreased particularly in TB patients and increased particularly after treatment. In some other previous study, it was found that all lipid parameters were significantly reduced in both newly diagnosed patients and relapse cases of Pulmonary TB in the study of Taparia P. et al.[20]

The limitation of the current study is that we selected a small population for our study consisting of 84 newly diagnosed TB patients. More study on this topic is required with large population to evaluate the link between anti-TB drugs and lipid's level concentration. Further studies should focus on the mechanism of action of anti-TB drugs on lipid profile that how these drugs aid in the increasing of cholesterol, HDL and LDL.

CONCLUSION

It is concluded that hypo lipidemia was found in newly diagnosed TB patients which would be a critical cause for the TB Infection. According to our study findings the overall difference of results before and after the TB treatment was significant. Intended for the better outcomes of anti-TB drugs needs to develop more enhanced guidelines including lipid level of patients. So, the main purpose of our study will help the researchers who needs to conduct more work on this topic at higher levels to evaluate that how MTB lowers the cholesterol, HDL and LDL level, and also supportive for the development of proper treatment of TB in Pakistan.

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ETHICAL APPROVAL: The study was approved by

Table 2: Mean difference of lipid profile in pulmonary tuberculosis patients before anti-tuberculosis treatment, after 6th and 10th weeks of the treatment with respect to age and gender (n=84)

	Before Treatment	6th week	10th week	p-value [a]	p-value [b]	p-value [c]	p-value [d]
Age, ≤ 34 years (n= 42)							
TC mg/dL	128.9 ± 27.2	146.2 ± 29.9	149.5 ± 30.6	< 0.001*	< 0.001*	0.252	< 0.001*
TG mg/dL	131.4 ± 38.3	133.1 ± 30.9	132.4 ± 21.9	0.714	0.868	0.860	0.061
HDL mg/dL	30.1 ± 12.6	36.2 ± 8.0	40.1 ± 7.2	0.008*	< 0.001*	< 0.001*	< 0.001*
LDL mg/dL	75.0 ± 20.8	86.4 ± 25.9	93.1 ± 31.2	0.002*	< 0.001*	0.037	< 0.001*
VLDL mg/dL	24.1 ± 7.5	24.3 ±6.6	23.7 ± 6.4	0.767	0.757	0.366	0.736
Age, > 34 years (n=42)							
TC mg/dL	126.9 ± 38.8	140.0 ± 25.8	142.3 ± 22.0	0.006*	0.006*	0.365	0.004*
TG mg/dL	128.2 ± 63.9	127.0 ± 25.9	125.3 ± 18.3	0.881	0.731	0.634	0.086
HDL mg/dL	28.3 ± 10.1	34.0 ± 6.4	39.1 ± 6.2	< 0.001*	< 0.001*	< 0.001*	< 0.001*
LDL mg/dL	74.0 ± 24.7	84.3 ± 22.0	87.7 ± 28.4	0.008*	0.005*	0.271	0.003*
VLDL mg/dL	23.3 ± 13.1	22.5 ± 6.0	21.5 ± 4.5	0.608	0.305	0.054	0.378
Gender, Males (n=44)							
TC mg/dL	130.9 ± 39.2	148.3 ± 30.3	152.5 ± 26.4	< 0.001*	< 0.001*	0.129	< 0.001*
TG mg/dL	136.7 ± 61.7	133.6 ± 27.7	131.5 ± 21.1	0.696	0.529	0.556	0.656
HDL mg/dL	29.5 ± 11.7	34.8 ± 7.8	39.2 ± 6.8	< 0.001*	< 0.001*	< 0.001*	< 0.001*
LDL mg/dL	75.1 ± 25.4	90.4 ± 24.7	98.4 ± 30.2	< 0.001*	< 0.001*	0.009*	< 0.001*
VLDL mg/dL	25.4 ± 12.8	24.8 ± 6.4	24.0 ± 6.1	0.698	0.402	0.098	0.477
Gender, Females (n=40)							
TC mg/dL	124.6 ± 25.5	137.3 ± 24.2	138.7 ± 25.5	< 0.001*	< 0.001*	0.611	< 0.001*
TG mg/dL	122.3 ± 39.2	126.1 ± 29.2	125.8 ± 19.5	0.434	0.568	0.946	0.665
HDL mg/dL	28.9 ± 11.2	35.4 ± 6.7	40.1 ± 6.6	0.002*	< 0.001*	< 0.001*	< 0.001*
LDL mg/dL	73.8 ± 19.5	79.9 ± 22.1	81.6 ± 27.1	0.071	0.038*	0.588	0.057
VLDL mg/dL	21.8 ± 7.2	21.9 ± 5.9	21.1 ± 4.7	0.896	0.547	0.293	0.605

HDL: High density lipoprotein, LDL: Low density lipoprotein, TC: Total cholesterol, TG: Triglyceride, VLDL: Very low density lipoprotein, a= baseline and 6th week, b= before and 10th week, c= 6th and 10th week, d= before, 6th and 10th week (RM-ANOVA) Paired t-test was applied between groups and Repeated Measure ANOVA was applied among before, 6th and 10th week
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Institutional Review Board, The University of Lahore (Reference No: IRB-UOL-FAHS/821-Vlll/2021).

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